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Original Article

Physiology Section

Study of Cardiovascular Reactivity to Mental Stress in Different Phases of Menstrual Cycle

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ABSTRACT

Background: It is a well known fact that normally female sex hormone levels fluctuate during the menstrual cycle. The presence of receptors for these hormones on both heart and blood vessels may also hint at variations in physiological functions during menstrual cycle. So this study was an attempt to determine whether the follicular and luteal phases of menstrual cycle are characterized by variations in cardiovascular parameters in the resting state and also examine changes in cardiovascular reactivity to mental stress challenge during both the phases of menstrual cycle.

Methodology: Thirty healthy females in the age group of 18-25 years with regular menstrual cycles fulfilling the inclusion criteria were examined for cardiovascular parameters (heart rate and blood pressures) at rest and their reactivity to mental stress during the follicular and luteal phase and were compared by using paired t-test. A p-value of <0.05 was considered as statistically significant.

Results: The women included in the study produced the well known reactivity to mental stress, in terms of blood pressure and heart rate increases, but the two phases of menstrual cycle were indistinguishable in so far as reactivity patterns were considered. The resting values of these cardiovascular parameters were also alike during the two phases.

Conclusion: We were unable to unearth any differences in resting and reactivity values of cardiovascular parameters during the course of a normal menstrual cycle. This shows that stress reactivity variations during different phases of menstrual cycle may not be due to variations in hormonal levels per se, but due to collusion of hormonal variations and unknown genetic influences.

Keywords: Cardiovascular reactivity, Follicular phase, Luteal phase, Mental stress

INTRODUCTION

The cyclical changes that occur in the female reproductive system are commonly referred to as the menstrual cycle. This is also associated with corresponding significant changes in multiple neurohumoral homeostatic mechanisms that regulate the cardiovascular system. It is becoming increasingly clear that gender has an influence on cardiovascular regulation at the cardiac and endothelial levels, as well as on autonomic regulation [1]. The presence of functional sex steroid hormone receptors in the cardiovascular system is well established as well as their expression in both heart and blood vessels have been recognized for decades [2].

Epidemiological studies have revealed that the incidence of cardiovascular disease is lower in premenopausal women than in age-matched men and postmenopausal women. Also estrogen replacement therapy is associated with a reduction in the incidence of coronary heart disease (CHD) as well as mortality from cardiovascular disease [3].

The various risk factors that contribute to cardiovascular disorders have to be identified and assimilated in order to adopt effective preventive strategies, especially in women where interplay of hormonal factors and different "penetrance" of risk factors occur [4].

One of the most active areas in psychosomatic research has focused on cardiovascular reactivity to mental stress [5,6]. It has been shown in a number of studies that during mental stress, there is an increase in sympathetic activity and a decrease in parasympathetic activity [7, 8]. This results in increased strain on the heart, immune and hormonal systems. This phenomenon suggests a mechanism through which psychological stress may exacerbate cardiac rhythm disturbances. Larger stress-induced blood pressure (BP) and Heart rate (HR) elevations are hypothesized to lead, over time, to elevation of the tonic BP level and the development of coronary artery disease. Investigation of cardiovascular responses to stress most often occurs in the laboratory through assessment of cardiovascular reactivity (CVR): BP and HR elevations occurring during the presentation of a discrete stressor [9].

Many studies have focused on the physiological reactivity to mental challenge in relationship to the risk of cardiovascular disease Some investigators have suggested that physiological functions fluctuate with the menstrual cycle [10,11], while others have observed no such menstrual phase effects [12,13]. In view of these conflicting results with regard to autonomic activity during various phases of menstrual cycle, we have decided to undertake this study and also use mental stress as an additional tool to explore the autonomic activity during the menstrual cycle.

MATERIALS AND METHODS

This longitudinal descriptive study was conducted in the Department of Physiology, Father Muller medical college Mangalore, Karnataka, India. The study population comprised of 30 healthy young females in the age group of 18-25 years meeting the following inclusion criteria.

Young healthy females in the age group of 18 -25 years, having regular menstrual cycles in the preceding one year and leading a sedentary life style were included and those females with a history of menstrual disorders, cardiovascular and respiratory disorders, those on medications that affect the activity of autonomic nervous system, cognitive performance and hypothalamo–pituitary ovarian axis and those with history of alcohol and tobacco consumption were excluded from the study.

Thirty two healthy females fulfilling the above inclusion criteria were initially recruited from the student population after a thorough clinical examination. Study was commenced only after obtaining the

Parameters	Follicular Phase	Luteal Phase	p-value
Heart Rate	75.1±8.7	77.68±10.92	0.49
SBP	106 ±8.84	107± 6.88	0.73
DBP	68.6± 9.5	68 ± 8.98	0.62
MAP	81.24± 8.88	81 ± 7.80	0.83

[Table/Fig-1]: Cardiovascular parameters during rest in both the phases of menstrual cycle

Parameters	Follicular Phase	Luteal Phase	p-value
Heart Rate	84.73± 9.44	87.87± 13.94	0.49
SBP	115.27 ±9.97	116 ± 7.13	0.63
DBP	77.2 ± 9.85	75.87 ± 9.79	0.35
MAP	89.89 ± 9.40	89.27 ± 8.40	0.64

[Table/Fig-2]: Cardiovascular parameters during mental stress in both the phases of menstrual cycle

Differences in	Follicular Phase	Luteal Phase	p-value
Heart Rate	9.52±5.31	10.97 ± 5.46	0.20
SBP	8.87± 3.95	9 ± 4.81	0.72
DBP	8.73 ± 4.99	7.8 ± 4.21	0.65
MAP	8.64 ± 3.94	8.27 ± 3.97	0.73

[Table/Fig-3]: Cardiovascular reactivity in both the phases of menstrual cycle

institutional ethical clearance. The informed consent was obtained from each participant after explaining the procedure in detail. All the individuals recruited for the study were asked to come to the physiology laboratory between 10-11 am after taking a light breakfast and abstinence from caffeinated drinks for at least 12 hours before coming for the recordings. Subjects were instructed to come for initial recordings between 5th to 10th day (follicular phase) of their menstrual cycle (counted from the first day of bleeding). Height and weight was measured using standard procedures and BMI calculated using Quetlet's index. Cardiart T6108 (BPL) was used for ECG recording and Stethoscope/Mercury Sphygmomanometer for recording of blood pressure.

Participants were asked to take rest for 15 minutes and then ECG leads were connected. ECG rhythm strip was generated in Lead II for resting heart rate calculation. Immediately the resting, Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) was also recorded. Subjects were then be asked to perform the serial subtraction task (a type of mental stress task) wherein the subject serially subtracts the number seven from a large number (eg 1024) and also vocalising the results of each step [14]. Lead II ECG and BP recordings were obtained during the mental stress task. Mean Arterial Pressure (MAP) was calculated from the BP recordings obtained during rest and mental stress. The changes observed in heart rate, SBP, DBP and MAP during mental stress were also calculated. Subjects were then asked to come after 15 days, that is between 20th - 25th day (luteal phase) of their menstrual cycle and the same procedures were repeated. The subjects were followed for another week to ten days and enquired about the onset of next cycle to confirm the luteal phase. If the next cycle was not started the whole procedure was repeated to take the fresh recordings. Out of 32 candidates, two subjects failed to report after 15 days for next reading. Hence their observations were kept outside the ambit of the study.

STATISTICAL ANALYSIS

The mean values of all the parameters recorded at rest and during mental stress in both the phases of menstrual cycle were compared using student's paired t-test. A p-value less than 0.05 was considered as significant. SPSS version 17 was used for statistical analysis.

RESULTS

The anthropometric data (mean ± SD) of all the 30 individuals who participated in the study are height - 158.96 ± 6.85 cms, weight - 56.75 ± 8.67 Kgs and Body Mass Index - 22.48 ± 3.24 Kg/m^2. The cardiovascular parameters such as heart rate, SBP, DBP and MAP which were recorded at the resting state during both the phases of menstrual cycle, did not show any significant difference [Table/Fig-1]. Same parameters exhibited an increase in the mean values when exposed to a mental stress by means of serial subtraction test in both the phases of menstrual cycle as shown in the [Table/Fig-2], but when these stress related increases in the cardiovascular parameters were compared between the two phases there was no statistically significant differences. However, these parameters exhibited a highly significant increase ($p<0.01$) in comparison with their resting values in follicular as well as in luteal phases of menstrual cycle.

The cardiovascular reactivity to mental stress was studied by calculating the differences in these parameters recorded during mental stress test and at resting state of both the phases of menstrual cycle. The mean values of these cardiovascular reactivity parameters were compared using paired t-test and were found to be statistically insignificant [Table/Fig-3].

Study	Sample size	Additional investigations done compared to present study	Out come
Sato N et al.,[2]	20	Menstrual cycle phases were determined by Basal body temperature and progesterone levels. Additionally HRV was also studied.	No change in HR and BP responses. But heart rate variability(HRV) study revealed predominant sympathetic activity in luteal phase
Sato N et al.,[11]	14	Menstrual cycle phases were determined by Basal body temperature. HRV was also analysed.	Same as above
Stoney CM et al.,[12]	15	All 3 phases (menstrual, follicular and luteal) were studied by estimating reproductive hormone levels and additional parameters such as low density lipoproteins, and total cholesterol were also studied	No change in HR and BP responses.
Weidner G et al.,[13]	16	Mood variation in follicular and luteal phases was also studied.	No change in HR and BP responses.
Carter JR et al.,[17]	11	Early follicular and mid luteal phases were studied. Luteinizing hormone, estrogen and progesterone levels were also estimated. An additional parameter muscular sympathetic activity (MSNA) was also studied.	No change in HR and BP responses. But a prolonged increase in postmental stress MSNA was observed in mid luteal phase

[Table/Fig-4]: The influence of menstrual cycle on cardiovascular reactivity to mental stress as observed in various other studies

DISCUSSION

It is an established fact that females have a less likelihood of developing cardiovascular disorders than males and it is equally true that this protective veil is prevalent only during the reproductive years of a female and is subsequently withdrawn postmenopausally [15]. The above statement stands on the fact that the female body during reproductive years is percolated by female sex hormones (estrogens and progesterone). The cardioprotective effects can be emphatically attributed to these hormones. However, levels of these hormones are not unvarying in premonopausal women and it fluctuates with the phases of menstrual cycle. So we took up this study to assess the cardiovascular reactivity in young Indian females in follicular and luteal phases of menstrual cycle by subjecting them to mental stress. Since during stress, hypothalamo pituitary adrenal axis (HPAA) regulates cortisol and adrenocorticotropic hormone (ACTH) levels and also ACTH secretion follows a circadian rhythm [16], hence to avoid variations we recorded all the parameters in the morning hours between 10- 11am.

The present study did not notice any differences in the basal heart rate between the phases, which is similar to the findings of many other studies [17-20]. Similarly the insignificant differences in basal SBP and DBP values in this study were also in concordance with the findings of Sato et al., [11]. Likewise a few studies have also reported similar results with respect to the mean arterial pressure [18,19,21]. This has been suggested to be because, the changes in HPA functioning over the course of the menstrual cycle are barely reflected in resting parameters and which may become prominent when the system is activated by a potent psychosocial stressor [16]. Hence we subjected the participants of this study to mental stress by employing the serial subtraction test and studied the effect of the same on these parameters in both phases.

The stressors such as mental challenge have been shown to induce beta-adrenergic activity with elevation in cardiac output, blood pressure and heart rate [11] and this can well explain our findings of a significant increase in these parameters on subjecting to the mental stress. Mental stress a known factor to cause an increase in sympathetic activity and decrease in parasympathetic activity [22]. Thus, subjecting an individual to mental stress should result in an increase in the cardiovascular reactivity. However, fluctuations in the hormonal levels are observed during the phases of menstrual cycle. Estrogen is predominant in follicular and progesterone in the luteal phase. Moreover, estrogen has been attributed with cardioprotective effects. Hence it increases the parasympathetic tone and progesterone blocks this action resulting in an increased sympathetic activity during luteal phase [20]. So it can be hypothesised that cardiovascular reactivity to mental stress should be more in luteal phase than the follicular phase in normally cycling women. This view was supported by findings of few previous studies [2,11]. Unlike this, the results in the present study did not show significant variations in cardiovascular reactivity to mental stress between two phases of the menstrual cycle. Similar observations regarding cardiovascular reactivity to stress were also observed by few previous studies [12,13,17] but with a lesser sample size than present study. These observations regarding stress induced cardiovascular reactivity and menstrual cycle in various other studies are provided in [Table/Fig-4]. These findings suggest that hormonal variations characteristic of the luteal and follicular phases do not assert an influence on common assessments of cardiovascular stress reactivity [13]. Moreover these hormonal fluctuations that occur during normal course of menstrual cycle may alter sympathetic outflow but not necessarily the transduction of sympathetic activity into vascular resistance. Carter et al., [17] also observed similar results in a study conducted on 11 females. The sample size of the present study is 30 which is comparatively better than these three studies.

An additional factor as far as stress reactivity is concerned is the ethnicity of the individual. In a study done on 33 healthy age- and weight-matched black and white normotensive women wherein the black women showed greater diastolic pressure and plasma epinephrine responses to stress during the follicular compared with the luteal phase of the menstrual cycle; but white women showed no significant changes in these variables [23].

CONCLUSION

The present study did not observe any significant differences in cardiovascular parameters neither at rest nor by subjecting young females to mental stress between the two phases of the menstrual cycle in normal cycling females. This could be because hormonal fluctuations that occur during normal course of menstrual cycle may modify the autonomic activity per se but not at the tissue level to modify the vascular resistance. Other than this there may be certain unknown factors which may contribute for these results such as genetic or environmental components which need to be explored. This shows that stress reactivity variations during different phases of menstrual cycle may not be due to variations in hormonal levels per se, but due to collusion of hormonal variations and unknown genetic influences.

The main limitation of our study is that we have not assessed the hormonal levels during the two phases of menstrual cycle. Moreover duration of exposure to stress is also a factor that can affect the result, as the exposure to stress in our study is of short duration, this may also have contributed for observations in our study. The stress in this study was induced in a laboratory setup, whereas the effects of real life stress may not necessarily mirror the effects observed here. Future studies taken up to throw more light on this topic should keep in mind these limitations.

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